Intrathecal morphine as sole analgesic during labour

PETER V SCOTT, FIONA E BOWEN, P CARTWRIGHT, B C MOHAN RAO, D DEELEY, H G WOTHERSPOON, I M A SUMREIN

Summary and conclusions

In 12 consecutive unselected patients admitted to a consultant maternity unit one single injection of subarachnoid morphine sulphate 1·5 mg abolished pain during the first stage of labour. Pain in the second stage was abolished in four patients and lessened in three. During the early puerperium, pain at the site of the episiotomy was much reduced. Side effects included itching of the face, nausea and vomiting, and frontal headache, but these were mild and simply treated. They were even less severe in the last four patients, in whom barbotage was not used in administering the morphine. The high rate of forceps delivery and caesarean section (three cases of each) was not thought to be associated with the use of intrathecal morphine.

These findings show that intrathecal morphine can abolish the pain of labour, whether spontaneous or induced, while preserving the mother's full awareness of labour and her co-operation in the second and third stages of labour. Further, controlled, trials are warranted.

Introduction

Intrathecal narcotics have been used in the management of various types of acute and chronic pain.[1] We report here a pilot study in 12 unselected women to determine the effect of intrathecal morphine on pain during labour.

Patients and methods

The 12 patients were fit young women aged 19 to 30 years who were admitted consecutively to the consultant maternity unit at Bromsgrove General Hospital. They were taking no drugs and had no known allergies. Their medical histories and physical examination showed no contraindications to lumbar puncture or subarachnoid block.[2] The experimental nature of the study was described in detail and informed consent obtained.

With the patient comfortably in the left lateral position, a pillow between her legs, and her hips flexed, the skin of the back from the shoulders to the buttocks was prepared with an antiseptic aerosol spray (Betadine) and allowed to dry. After stringent aseptic precautions by the scrubbed, doubly-gloved, masked, and gowned operator (PVS) the skin between the spines of the third and fourth lumbar vertebrae, and, in one case, between L4 and L5, was infiltrated with 2 ml lignocaine.

After making a small (2-mm) incision in the anaesthetised skin, a 22-gauge disposable spinal needle was inserted into the subarachnoid space through a Sise introducer. The stylet was removed, a free flow of cerebrospinal fluid obtained, and the needle rotated through 360° to confirm that its bevel was entirely within the space.[2] The stylet was replaced. The operator's second pair of gloves was removed by an assistant.

A 1·0-ml disposable plastic syringe containing specially formulated sterile morphine without preservative, bactericide, or antioxidant was attached to the spinal needle. (The 1·0-ml ampoule of morphine contained 10·0 mg/ml morphine sulphate in normal saline, specific gravity 1·0097, pH 5·6-5·7, sterilised by autoclaving. Morphine which contains a preservative, a bactericide, or an antioxidant must never be used intrathecally. Cerebrospinal fluid itself has a specific gravity of 1·003-1·009, pH 7·6.[2])

Morphine 0·15 ml—that is, 1·5 mg—was then injected into the cerebrospinal fluid by barbotage.[2] The spinal needle was withdrawn and a sterile elastoplast dressing applied to the skin incision. Most patients then elected to lie supine. Induction of labour, if required, was performed 15-90 minutes later. In the last four cases barbotage was omitted.

Results and comments

Details of the mothers and their babies are given in the table. All mothers except two (cases 7 and 9) were normotensive and had been so throughout their pregnancies. No significant changes in blood pressure were seen before, during, or after intrathecal morphine. Pulse rate, respiratory depth (Wright's respirometer), respiratory frequency, and temperature were equally stable. There was no loss of tone in striated muscle and no apparent depression of uterine contractions. Blood loss throughout labour was in the normal range.

One patient (case 1) did not realise that she was in labour until the fetal head presented at the vulva, while another (case 2) did not realise it until the onset of the second stage. The remaining patients felt uterine contractions during the first stage, but they were painless as judged by patient and midwife. The pain of the second stage was abolished in one primigravida (case 4) and three multiparas (cases 6, 8, and 9) and appeared to be considerably diminished in three multiparas. There was no loss of the "pushing reflex," so allowing full maternal co-operation for the progress of the second stage.

Throughout the labours, which were conducted under oxytocin infusion, the fetal heart rate and uterine contractions were monitored continuously (Sonicaid fetal monitor, model FM2). There was no evidence of fetal distress in any patient except one, in whom the fetal heart rate fell to 80 beats/min, with late decelerations. The baby was delivered by immediate caesarean section.

After the six spontaneous deliveries Apgar scores at one minute were 9,7,6,8,9, and 9; at five minutes they were 10,8,8,10,10, and 10 (see table). Apgar scores in babies delivered by forceps were 8,6, and 6 at one minute, and 10,8, and 10 at five minutes. One baby delivered by outlet forceps for delay in the second stage (case 12) was intubated and the lungs ventilated for one minute with oxygen; naloxone 0·04 mg was given. The babies delivered by caesarean section had Apgar scores of 8,9, and 9 at one minute and 10 in all three at five minutes.

Caesarean section was performed in three patients. Less general anaesthetic and less muscle relaxant were used than normal. (Induction sequence: pre-oxygenation; thiopentone sodium 2·5% 250 mg; suxamethonium chloride 75 mg; cricoid pressure; intubation, oral endotracheal tube.) The lungs were ventilated mechanically at 10 l/min (Manley Pulmovent MPP Minute Volume Divider) at a tidal volume of 800 ml (Wright's respirometer) with a 50:50 mixture of oxygen and nitrous oxide. During the induction-delivery interval one woman (case 3) also received 0·3% trichloroethylene from a calibrated vaporiser. After delivery the respired gas mixture was changed to 25:75 oxygen:nitrous oxide. Two increments of 12·5 mg suxamethonium were then needed to maintain full muscle relaxation. No analgesics other than nitrous oxide were necessary. (The pupils were constricted throughout.) The patients' inhaled and exhaled carbon dioxide concentrations were continuously measured. Carbon

Department of Anaesthetics, Bromsgrove General Hospital, Bromsgrove, Worcestershire B61 0BB
PETER V SCOTT, MB, FFARCS, consultant anaesthetist
FIONA E BOWEN, MB, DA, registrar
P CARTWRIGHT, MB, senior house officer
B C MOHAN RAO, MB, senior house officer
D DEELEY, MB, DA, senior house officer

Department of Obstetrics, Bromsgrove General Hospital, Bromsgrove, Worcestershire, B61 0BB
H G WOTHERSPOON, MB, FRCOG, consultant obstetrician
I M A SUMREIN, MD, MRCOG, registrar

Details of the 12 mothers and their babies

Case No	Mother						Baby		
	Age (years)	Para	Gestation (weeks)	Weight (kg)	Height (cm)	Method of delivery	Apgar score 1 min	Apgar score 5 min	Birth weight (g)
1	22	1+1	40	58·0	153	Spontaneous, vertex	9	10	2970
2	22	1+1	>40	61·3	151	Spontaneous, vertex	7	8	2700
3	23	0+0	?40	62·6	154	LSCS, breech	8	10	3090
4	22	0+0	?40	72·0	160	Spontaneous, vertex	6†	8	3120
5	20	0+0	?42	76·6	150	LSCS, vertex	9	10	4150
6	24	1+0	>41	99·0	170	Spontaneous, vertex	8	10	3610
7	23	0+0	39	77·6	166	LSCS, vertex	9	10	3490
8*	27	2+1	40	77·5	160	Spontaneous, vertex	9	10	3510
9	29	1+0	42	68·3	161	Spontaneous, vertex	9	10	3264
10	19	0+0	41	59·5	149·5	Outlet forceps, vertex	8	10	3400
11	30	0+0	42	62·2	152	Kielland's forceps, left occipitotransverse	6	8	3260
12	24	0+1	41	76·7	160	Outlet forceps, vertex	6‡	10	3500

*Two previous forceps deliveries under epidural anaesthesia.
†Promethazine given at 5 cm cervical dilatation. The sedative effect of this drug might have accounted for the low Apgar score at 1 min.
‡Intubated.
LSCS = Lower segment caesarean section.

dioxide was added to the respired mixture to maintain a maternal end-tidal CO_2 concentration of 5·5-6·0%, equivalent to a maternal $PaCO_2$ of 5·19-5·75 kPa (39-43 mm Hg). The patients' blood pressures and electrocardiograms were stable throughout surgery. The pulse rates never exceeded 100 beats/min, and there were no cardiac arrhythmias. Recovery from anaesthesia was complete within two minutes of withdrawing nitrous oxide and substituting 100% oxygen. No patient recollected the surgery. Only one needed analgesia post-operatively. She was given Cyclimorph 10 (1 ml) 18 hours after the caesarean section—that is, 25 hours after her original injection of intrathecal morphine.

Side effects—About 30 minutes after injection of intrathecal morphine all patients experienced itching of the mouth, face, eyes, and particularly the nose. These symptoms seem almost pathognomonic of morphine spinal analgesia. (The nasal itching was similar to that experienced after the administration of intravenous nikethamide.) The itching gradually waned over a few hours, although five patients had mild irritation of the face, arms, and nose on the first and second days of the peurperium. Again about 30 minutes after injection, the first seven patients complained of feeling "hot," though their body temperatures were normal. The feeling was shortlived. Nine patients became nauseated, and five of these vomited. The vomiting stopped in four patients after intravenous metoclopramide 10·0 mg and in the fifth after intravenous promethazine 25·0 mg. One patient (case 8) vomited and felt nauseated 15 minutes after completing the third stage. Naloxone 0·4 mg intravenously abolished both nausea and vomiting within five minutes, and the patient seemed to become more alert. One patient (case 2) experienced transient diplopia 40 minutes after intrathecal morphine. The urinary bladders of four patients required catheterisation on one occasion, and only one, during labour.

Puerperium—The first eight patients were nursed supine for 24 hours and the last four for 12 hours, firstly with two pillows, then with three. They were allowed out of bed only to use a commode (which was brought to the bedside) or a bidet. Three patients developed frontal headaches 24 to 48 hours after delivery. (True spinal headaches tend to be occipital.) Aspirin was the only treatment necessary. The last four patients in the series, in whom barbotage was not performed, did not complain of headache, and the other side effects were less troublesome. Two patients did not require local anaesthesia for suture of the episiotomy, and pain at the site of episiotomy seemed to be much reduced in the early puerperium. It was our clinical impression that neither the ability nor the desire to breast-feed was affected.

Discussion

In this pilot study intrathecal morphine sulphate 1·5 mg in 0·15 ml normal saline abolished pain during the first stage of labour and abolished or lessened it during the second stage and early puerperium. These advantages were gained without the complications sometimes seen with the standard techniques of epidural analgesia.[3] Side effects were mild, simply treated and probably dose related. The facial itching might be a central effect of intrathecal morphine, mediated through internuncial neurones in the substantia gelatinosa of the spinal cord. The substantia gelatinosa is continuous in the upper cervical region of the cord with the nucleus of the trigeminal nerve.

Side effects can be reduced by omitting barbotage. In one subsequent patient not reported here they were reduced when only 1·0 mg morphine was used. Side effects might also be reduced by using opiates other than morphine: fentanyl, pethidine, buprenorphine, or, when they become available, the synthetic endorphins; by preoperative medication—for example, a long-acting antipruritic and antiemetic such as promethazine; or by treating severe persisting symptoms (especially nausea and vomiting) with intramuscular naloxone. Naloxone reverses some of the side effects of intrathecal morphine without seeming to antagonise the analgesic effects (J S Robinson, personal communication, 1980).

Post-spinal headache must always be a risk. Although our patients have so far remained immune, spinal headache occurs in 3-20% of patients who receive intrathecal (local) anaesthetics. Nor is it rare after simple lumbar puncture.[2] We now use a Whitacre-type 22-gauge spinal needle; but it may be wiser to use the slimmest spinal needle available (25 gauge). We try to reduce the risk of spinal headache by gradual mobilisation, encouraging a high fluid intake, and using a tight, elastic abdominal binder (Tubigrip) to maintain a high intra-abdominal pressure during the early puerperium. The binder has an added advantage in that patients actually like to wear it.

Whatever techniques are used, and whatever precautions are taken, absolute antisepsis and asepsis are mandatory. We now inject the morphine through an epidural bacterial filter (Portex) to make assurance doubly sure. Under no circumstances should the dose of 1·0-1·5 mg morphine be exceeded. There is a theoretical risk that some morphine may diffuse through the foramen magnum and enter the fourth ventricle of the brain. Finally, and most important, no morphine should be used which has not been specially formulated to exclude preservative, bactericide, or antioxidant. The morphine should be sterilised by autoclaving.

The number of patients in this series was very small. There were three instrumental deliveries (incidence 25%) and three

caesarean sections (incidence 25%). We do not think that the apparently high rate of surgical interference bears any relation to the use of intrathecal morphine, but it is too early yet to be sure. Our next eight patients (not reported here) all delivered spontaneously, thus reducing the incidence of both forceps delivery and caesarean section to 15%. In 1979 the incidence of forceps delivery among 1305 live births was 14·7% and the incidence of caesarean section 13·8%. The incidence of forceps delivery under epidural analgesia varies from 50% to 60%.

The use of intrathecal morphine in labour owes its origin to the basic work of Snyder[4 5] and to reports on the use of intrathecal narcotics for managing various types of acute and chronic pain.[1] Epidural morphine has so far failed to relieve the pain of labour, perhaps because "the increased vascularity of the epidural space in pregnancy is responsible for rapid clearance of injected morphine so that effective concentrations of morphine in the cerebrospinal fluid and spinal cord are not reached."[6]

We consider that the use of intrathecal morphine to treat and prevent the pain of labour deserves a controlled study. If that study confirms our results the implications for the pregnant woman, for patients undergoing many types of surgery, and for the disciplines of obstetrics, neonatology, and especially anaesthetics, might well be profound.

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SHORT REPORTS

Hydrallazine in hypertension: Is there a safe dose?

The early use of hydrallazine for treating hypertension was associated with two problems: reflex mediated haemodynamic effects, and the development of a lupus-like syndrome.[1] The haemodynamic effects may be limited by combining hydrallazine with β-adrenergic blockade, and such combinations are now widely used with a consequently greater risk of hydrallazine toxicity.

Hydrallazine is excreted mainly as the acetylated metabolite, and the population is divided into rapid and slow acetylators. Hydrallazine toxicity depends on exposure to free drug and occurs more frequently in slow acetylators[2] although the dose and duration of treatment are also important factors. Present recommendations are that the maximum daily dose of hydrallazine should not exceed 200 mg.[3]

To assess the value of current advice we have studied the incidence of lupus syndrome in patients treated with hydrallazine in conventional doses and have also assessed the incidence of positive antinuclear factor titres in asymptomatic hypertensive patients.

Patients, methods, and results

Patients who attended the Leicester Hypertension Clinic from 1974 to 1979 and received hydrallazine were reviewed for evidence of hydrallazine toxicity. In addition, antinuclear factor (ANF) titres were measured in 61 asymptomatic patients on combination therapy (hydrallazine, β-adrenergic blocker, and diuretic) and in 37 hypertensive patients treated with only β-adrenergic blocker and diuretic. No patient was receiving other drugs or had a disease likely to give a positive ANF titre. Acetylation phenotype was determined in all patients treated with hydrallazine who were studied.[4] Statistical analysis was by χ^2 and Mann-Whitney U tests.

Six patients out of 200 patients receiving hydrallazine developed a lupus-like syndrome (table). All were slow acetylators and had not received more than 200 mg hydrallazine a day. Mean duration of treatment was 19·5 months (11-25 months). Presenting features included arthritis in five, rashes in two, and all showed marked weight loss before other symptoms. All had normal renal function. The ANF titre was raised in all six patients when they developed symptoms; DNA antibody, however, was often normal, only later becoming appreciably raised in three. When hydrallazine was discontinued clinical features resolved rapidly in four, one required non-steroid anti-inflammatory drugs and was symptom free at six months, and one has required steroids for over 12 months.

The two groups of asymptomatic hypertensive patients did not differ in age, sex ratio, dosage of β-adrenergic blocker, or renal function. There were three positive ANF titres in those patients not taking hydrallazine, all of low titre (1/16), whereas in the hydrallazine-treated group 22 had positive ANF titres (seven at 1/16, 12 at 1/64, and three at 1/256). The frequency and distribution of positive ANF titres was significantly different between the two groups ($p<0·005$). In the group treated with hydrallazine positive ANF titres were more frequent in slow compared with rapid acetylators (20/43 *v* 2/18; $p<0·025$), but were not related to dose, duration of treatment, or renal function. Positive ANF titres were more common in women patients ($p<0·05$ for the groups combined).

Comment

Three per cent of patients developed a lupus-like syndrome while taking hydrallazine: all were slow acetylators and had not received more than 200 mg daily. The clinical features were mild in four, but symptoms persisted for several months in the other two, one of whom required steroids. These findings are in contrast with present

Clinical and biochemical details of hydrallazine toxic patients

Case No	Sex	Age	Hydrallazine		Symptoms	ANF titre	DNA antibody (normal<25 IU/ml)	Effect of withdrawal
			Dose (mg)	Duration (months)				
1	F	36	200	17	Rash	>1/4000	Negative	Cleared rapidly
2	M	53	200	24	Arthritis/myalgia Rash	>1/4000	44	Cleared slowly (6 months)
3	M	47	200	25	Arthralgia	>1/4000	12	Cleared rapidly
4	F	59	200	11	Arthritis	1/1000	34	Cleared rapidly
5	F	55	200	24	Arthritis	1/1000	24	Cleared rapidly
6	F	57	150	16	Arthritis	1/256	53	Persisted, on steroids